REMARKS

Claims 1, 4-10, 16-17, 19-20, 23-26, 31-35, 39-41, and 71-72 are currently pending in the above-referenced application. Claims 1, 4-10, 16-17, 25, 35, 40, and 71 have been amended to further clarify the invention. No new matter is introduced by these amendments; these amendments find support in the specification in at least ¶¶10, 19, 28, and 29.

Claims 2-3, 11-15, 18, 21-22, 27-30, 36-38, and 42-70 have been cancelled. Applicant reserves the right to prosecute the subject matter of the cancelled claims in one or more continuation or continuation-in-part applications.

Response To Rejections Of Claims 1, 4-10, 16, 17, 19, 20, 23, 24, 35, 39-41, 71, and 72 Under 35 U.S.C. § 112, ¶1

Claims 1, 4-10, 16, 17, 19, 20, 23, 24, 35, 39-41, 71, and 72 have been rejected under 35 U.S.C. § 112, ¶1 as failing to comply with the written description requirement because the Examiner believes that the specification does not provide adequate support for "an agent." Applicants respectfully disagree with this rejection. However, in order to expedite the prosecution of the instant application, applicants have amended the cited claims to refer to "an inhibitory agent," as supported by the instant specification. *See, e.g.,* paragraphs 10, 19, 28, and 29. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, ¶1 is respectfully requested.

Response To Rejections Of Claims 1, 4-10, 16, 17, 19, 20, 23, 35, and 39 Under 35 U.S.C. § 112, ¶2

Claims 1, 4-10, 16, 17, 19, 20, 23, 35, and 39 have been rejected under 35 U.S.C. § 112, ¶2 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully disagree with this rejection. However, in order to expedite prosecution of the instant claims to allowance, applicants have amended these claims to address the Examiner's concerns. The claim amendments are supported by the instant specification, for example, in paragraphs 10, 19, 28, and 29.

In particular, claim 1 has been rejected under 35 U.S.C. § 112, ¶2 as allegedly being incomplete for omitting essential elements. The Examiner contends that the size range of "0.03-1 micron in size" does not disclose an upper limit to the size of the agent encapsulated within a suitable carrier. Applicants respectfully disagree with the Examiner's contention and assert that the skilled person would clearly read this phrase as defining an upper and lower limit (i.e., a range). However, in order to expedite prosecution, applicants have amended these claims in accordance with the language suggested by the Examiner. These amendments are supported in the instant specification, for example, in paragraphs 15 and 27. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, ¶2 is respectfully requested.

Claims 4-10, 16, 17, 19, 23, and 24 have been rejected under 35 U.S.C. § 112, ¶2 as being indefinite because of insufficient antecedent basis for the limitation of "the method as in one of the claims 1-3" because claims 2 and 3 have been cancelled. Applicants have amended these claims to address the Examiner's concerns.

Reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, ¶2 is respectfully requested.

Response To Rejection Of Claims 1, 4-10, 16, 17, 19, 20, 23-26, 31-35, 39-41, 71, and 72 Under 35 U.S.C. § 103(a)

Claims 1, 4-10, 16, 17, 19, 20, 23-26, 31-35, 39-41, 71, and 72 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Pennanen et al. ("Effect of Liposomal and Free Bisphosphonates on the IL-1β, IL-6, and TNF-α Secretion from RAW 264 Cells In Vitro," *Pharmaceutical Research*, Vol. 12, No. 6, pp. 916-922, 1995) and Hack, et al. (U.S. Patent No. 6,090,777) in view of Ylitalo ("Bisphosphonates and Atherosclerosis," *Gen. Pharmacology*, Vol. 35, pp. 287-296, 2002) and Hope, et al. (U.S. Patent No. 6,139,871). Applicants respectfully traverse this rejection.

Pennanen describes an *in vitro* study wherein liposome-bisphosphonates inhibited the secretion of proinflammatory cytokines, such as IL-1β, IL-6, and TNF-α, from the RAW 264 cell line. Pennanen fails to teach or suggest a method of treating a patient having an acute myocardial infarction. Pennanen fails to teach or suggest any correlation between an AMI and liposomal bisphosphonates. No common sense reason exists (nor had the Examiner identified one) without the benefit of hindsight as to why the skilled person would look to Pennanen in an attempt to treat an AMI. In fact, the only condition correlated with the Pennanen study relates to arthritic joints (p. 921). Pennanen suggests that "chronic inflammatory diseases" may benefit from bisphosphonate liposomes, which indeed is quite the opposite from an acute myocardial infarction.

Hack describes administration of an exogeneous C-1 esterase for the treatment of an acute myocardial infarction. (*See* Hack at 7:31-55). Hack does not teach or suggest the use of bisphosphonate-liposomes nor would the skilled person look to bisphosphonate-liposomes over the use of exogenous C-1 esterase in view of Hack and Pennanen. At best, Pennanen suggests bisphosphonate-liposomes may be useful in treating chronic inflammatory conditions but does not give any hint that an acute condition such as AMI could be so treated. Based upon Hack, one skilled in the art would have no common sense reason for substituting bisphosphonate-liposomes for the C-1 esterase inhibitor taught by Hack to treat AMI.

The Ylitalo reference does not remedy the deficiencies of the Pennanen and Hack combination. Ylitalo describes a method of treating atherosclerosis, but does not teach or suggest a method of treating a patient having an acute myocardial infarction. The physical events that occur during an acute myocardial infarction are completely different from those occurring during atherosclerosis and Ylitalo, alone or in combination with Pennanen and/or Hack, teach or suggest that methods used for treating atherosclerosis can be effective in treating a patient undergoing an acute myocardial infarction.

Hope, like Ylitalo, relates to a treatment for atherosclerosis and does not teach or suggest a method of treating a patient having an acute myocardial infarction, as recited in the instant claims.

The combination of these four references does not lead one skilled in the art to reach the claimed invention. None of these references, alone or in combination, teach or suggest a treatment for an acute myocardial infarction using liposomal-

bisphosphonates. Ylitalo, Hope, and Pennanen describe the use of bisphosphonates to treat chronic progressive diseases which are different from acute diseases in etiology and treatment regimes. While chronic diseases require treatments that must be tolerated over long periods of time, acute disease conditions require quick and sometimes extreme treatments. One skilled in the art would not look to treatments for long term progressive diseases for treatments of acute situations. As previously discussed, the physical events that occur during an acute myocardial infarction are completely different from those occurring during chronic diseases such as atherosclerosis. (See Response to Non-Final Office Action filed July 28, 2008.) Furthermore, as the Examiner admits there is no discussion in Pennanen as to treating a patient having an acute myocardial infarction. (See page 6 of the pending Final Office Action dated February 9, 2009.) While Hack teaches a method of treatment for AMI, this reference does not teach the use of liposomal-bisphosphonates for that treatment. Hack teaches the use of a very specific compound, exogenous C-1 esterase. A person of ordinary skill in the art would not be motivated to adopt some of the teachings of Hack (i.e., use of an inflammation inhibitor), but abandon the specific compound (i.e., exogenous C-1 esterase) taught by the Hack reference. One skilled in the art would recognize the benefit of the anti-inflammatory compound in Hack but would have no motivation, suggestion, or common sense reason to abandon Hack's specific compound and instead use a liposomal-bisphosphonate which is disclosed in an unrelated reference for treating chronic diseases. There is no common sense reason or motivation to combine the cited references to treat a patient having an AMI. The only

reasonable excuse for combining the four cited references, as the Examiner has, is by using impermissible hindsight.

For these reasons, applicants respectfully request that the Examiner withdraw this § 103(a) rejection of Claims 1, 4-10, 16, 17, 19, 20, 23-26, 31-35, 39-41, 71, and 72.

CONCLUSION

For the foregoing reasons, it is respectfully submitted that the pending claims are in condition of allowance. Favorable reconsideration and allowance of Claims 1, 4-10, 16-17, 19-20, 23-26, 31-35, 39-41, and 71-72 is respectively requested.

If any issues remain, or if the Examiner has any suggestions for expediting allowance of the application, the Examiner is invited to contact the undersigned attorney.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-4387**, Order No. 92114.005US1.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-4387**, Order No. 92114.005US1.

Respectfully submitted,

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